

1. A purified preparation of immunologically privileged cells which express at least one protein not normally expressed by said cells.
- 5 2. The cells of claim 1, which are intermediate lobe pituitary cells.
3. The cells of claim 1, wherein said protein is expressed from a heterologous nucleic acid sequence inserted into the cell.
- 10 4. The cells of claim 1, wherein expression of said protein is operatively linked to a control region other than the one which normally controls it.
- 15 5. The cells of claim 2, wherein expression of said protein is operatively linked to a control region which is active in or specific for the intermediate lobe pituitary cell.
6. The cells of claim 2, wherein said protein is from a first species and the intermediate lobe pituitary cells is from a second species.
- 20 7. Intermediate lobe pituitary cells which express insulin from an insulin-encoding nucleic acid sequence.
8. The cells of claim 7, wherein the insulin-encoding nucleic acid sequence is operatively linked to a control region other than the insulin control region.
- 25 9. The cells of claim 8, wherein said insulin-encoding nucleic acid sequence encodes human insulin.
10. The cells of claim 7, wherein said intermediate lobe pituitary cells are chosen from: fetal or non-fetal, human or non-human cells.
- 30 11. The cells of claim 7, wherein the insulin-encoding nucleic acid encodes human insulin and the intermediate lobe pituitary cells are from another species.
- 35 12. The cells of claim 7, wherein said cells further express another protein which is not normally expressed in intermediate lobe pituitary cells, and which mediates glucose stimulated insulin secretion.

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13. The cells of claim 12, wherein said protein promotes the transport of glucose across the plasma membrane such that insulin release by the cells is modulated by glucose levels.

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14. The cells of claim 12, wherein said cells express glucokinase with a high Km for glucose.

10 15. The cells of claim 14, wherein said cells further express an ion channel which mediates the glucose stimulated insulin secretion.

16. The cells of claim 12, wherein said cells further express GLP-1.

15 17. The cells of claim 7 which are encapsulated within a non-antigenic compound.

18. The cells of claim 17 wherein the compound is a polymer.

20 19. The cells of claim 17 wherein said compound is hydrogel, olginate or semipermeable fiber.

20 20. Immunologically privileged cells which express human insulin, wherein said cells include:

25 an insulin-encoding nucleic acid sequence operatively linked to a control region which allows expression in said cells;

a nucleic acid sequence which encodes GLUT-2 operatively linked to a control region which allows expression in said cells;

30 a nucleic acid sequence which encodes the  $\beta$ -cell isoform of glucokinase operatively linked to a control region which allows expression in said cells; and

a nucleic acid sequence which encodes an ion channel which mediates the expression of insulin operatively linked to a control region which allows expression in said cells.

21. The cells of claim 20, further including a nucleic acid which encodes GLP-1.

22. The cells of claim 20 which are intermediate lobe pituitary cells.
23. Intermediate lobe pituitary cells which express human insulin, wherein said cells include:
- 5        a heterologous insulin-encoding nucleic acid sequence operatively linked to a control region other than the insulin control region;
- a nucleic acid sequence which encodes GLUT-2 operatively linked to a control region other than the GLUT-2 control region;
- a nucleic acid sequence which encodes the β-cell isoform of glucokinase
- 10      operatively linked to a control region other than the glucokinase control region; and
- a nucleic acid sequence which encodes an ion channel which mediates glucose-sensitive insulin secretion operatively linked to a control region which allows expression in intermediate lobe pituitary cells.
- 15      24. Intermediate lobe pituitary cells which express human insulin, wherein said cells include:
- a insulin-encoding nucleic acid sequence operatively linked to a control region which allows expression in intermediate lobe pituitary cells;
- a nucleic acid sequence which encodes GLUT-2 operatively linked to a control
- 20      region which allows expression in intermediate lobe pituitary cells;
- a nucleic acid sequence which encodes the β-cell isoform of glucokinase operatively linked to a control region which allows expression in intermediate lobe pituitary cells; and
- a nucleic acid sequence which encodes a K<sup>+</sup>/ATP ion channel which mediates
- 25      the expression of insulin operatively linked to a control region which allows expression in intermediate lobe pituitary cells.
- 30      25. The cells of claim 24, further including a nucleic acid which encodes GLP-1 operatively linked to a control region which allows expression in intermediate lobe pituitary cells.
26. A method of producing a protein in a subject *in vivo* comprising introducing into the subject an immunologically privileged cell which expresses the protein.

27. The method of claim 26, wherein said cell is an intermediate lobe pituitary cell and the protein is one which is not normally expressed therein.

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28. The method of claim 27, wherein said intermediate lobe pituitary cells includes a nucleic acid sequence which encodes a protein not normally expressed by an intermediate lobe pituitary cell operatively linked to a heterologous control region which controls expression of the nucleic acid in the intermediate lobe pituitary cell.

29. The method of claim 28, wherein said protein is insulin.

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30. The method of claim 27, wherein said intermediate lobe pituitary cell is an autologous cell, an allogenic cell, or a xenogenic cell.

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31. The method of claim 28, wherein said subject is a human and the intermediate lobe pituitary cell is an autologous cell, an allogenic cell or a xenogenic cell.

32. A transgenic animal expressing at least one protein not normally expressed in intermediate lobe pituitary cells.

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33. The transgenic animal of claim 32 which is a pig.

34. The transgenic animal of claim 33 wherein the protein is insulin.

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35. The transgenic animal of claim 34 wherein the expression of insulin is controlled in a glucose stimulated insulin secreting manner.

36. A subject which has an intermediate lobe pituitary cell which express a peptide not normally expressed in intermediate lobe pituitary cells.

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37. The subject of claim 36, wherein the cell expresses insulin.

38. The subject of claim 37, the expression of insulin is controlled in a glucose stimulated insulin secreting manner.

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39. A method of treating a subject in need of a protein, comprising introducing immunologically privileged cells which express the protein systemically.

5 40. The method of claim 39 wherein the cells are intermediate lobe pituitary cells and the protein is insulin.

41. The method of claim 40 wherein the expression of insulin is controlled in a glucose stimulated insulin secreting manner.

10 42. A method of treating an individual suffering from diabetes or insulin deficiency comprising introducing intermediate lobe pituitary cells which express insulin in a glucose stimulated insulin secreting manner systemically.

15 43. The method of claim 42 wherein the cells further express glucokinase, GLUT-2 and a K<sup>+</sup>/ATP ion channel.

44. The method of claim 42 wherein the cells further express GLP-1.

20 45. A method of expressing a protein not normally expressed in intermediate lobe pituitary cells comprising transfecting, *in vivo*, said cells with a nucleotide sequence encoding the protein.

46. The method of claim 45, wherein the protein is insulin.

25 47. The method of claim 46, further including transfecting said cells with additional nucleotide sequences encoding one or more additional proteins which control expression of insulin in a glucose stimulated insulin secreting manner.

30 48. The method of claim 47, wherein the additional nucleotide sequences encode the following proteins: the β-cell isoform of glucokinase, GLUT-2, and a K<sup>+</sup> ATP ion channel.

49. The method of claim 47, wherein the additional nucleotide sequences encode GLP-1.

50. Intermediate lobe pituitary cells which have been transfected to express insulin, and which have further been transfected with nucleotide sequences encoding other proteins, comprising nucleotide sequences encoding:  
the  $\beta$ -cell isoform of glucokinase operatively linked to a control region to allow expression in such cells;  
GLUT-2 operatively linked to a control region to allow expression in such cells; and A K $^{+}$ /ATP ion channel which mediates expression of insulin operatively linked to a control region to allow expression in such cells.
- 5 10 51. The method of claim 47, wherein the nucleotide sequences also encode GLP-1.
- 15 52. A method of expressing a protein in immunologically privileged cells not normally expressing said protein comprising transfecting, *in vivo*, said cells with a nucleotide sequence encoding said protein.
53. The method of claim 52, wherein the protein is insulin.
- 20 54. The method of claim 53, further including transfecting said cells with additional nucleotide sequences encoding one or more additional proteins which control expression of insulin in a glucose stimulated insulin secreting manner.
55. The method of claim 53, wherein the additional nucleotide sequences encode the  $\beta$ -cell isoform of glucokinase, GLUT-2 and a K $^{+}$ /ATP ion channel.
- 25 56. The method of claim 47, wherein the additional nucleotide sequences also encode GLP-1.
- 30 57. A method of expressing insulin in cells which do not normally express insulin comprising transfecting, *in vivo*, said cells with a nucleotide sequence encoding insulin and with additional nucleotide sequences encoding one or more additional proteins which control expression of insulin in a glucose stimulated insulin secreting manner.

58. The method of claim 57 wherein the additional nucleotide sequences encode the  $\beta$ -cell isoform of glucokinase, GLUT-2 and a K<sup>+</sup>/ATP ion channel.

59. The method of claim 47, wherein the additional nucleotide sequences also  
5 encode GLP-1.

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